

Notice of Allowability**Application No.**

09/716,320

Examiner

Jane Zara

Applicant(s)

CHANG ET AL.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 1-23-04.
2. ☒ The allowed claim(s) is/are 1-32.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☒ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Barbara Ernst on or about March 30, 2004.

The application has been amended as follows:

In claim 1, line 4, "comprising" has been replaced with --consisting of--.

Claim 3 (currently rewritten): A method for reducing radiation or drug resistance of a human cell which does not overexpress *Her-2*, said method comprising introducing into the cell an antisense nucleic acid in an amount effective to reduce said radiation or drug resistance, which antisense nucleic acid comprises a segment that is complementary to *HER-2* and inhibits *HER-2* expression.

Claim 7 (currently rewritten): A method for treating a person with a disease wherein said person is resistant to radiation or drug treatment of said disease, wherein resistance to said radiation or drug treatment is not a result of overexpression of *HER-2*,

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said method comprising administering to said person an antisense nucleic acid in an amount effective to decrease said resistance to radiation or drug treatment, which antisense nucleic acid comprises a segment complementary to HER-2 and inhibits HER-2 expression.

Claim 12 (currently rewritten): A method for reducing radiation or drug resistance of a human cell which overexpresses HER-2, said method comprising introducing into the cell an antisense nucleic acid in an amount effective to reduce said radiation or drug resistance, which antisense nucleic acid comprises a segment complementary to HER-2 and inhibits HER-2 expression.

In claim 15, line 1, "16" has been replaced with --12--.

Claim 16 (currently rewritten): A method for treating a person with a disease wherein said person is resistant to radiation or drug treatment of said disease, wherein resistance to said radiation or drug treatment is a result of overexpression of HER-2, said method comprising administering to said person an antisense nucleic acid in an amount effective to reduce said radiation or drug resistance, which antisense nucleic acid comprises a segment complementary to HER-2 and inhibits HER-2 expression.

Examiner's Reasons for Allowance

The following is an examiner's statement of reasons for allowance: The claimed invention is free of the prior art of record because the prior art of record does not teach or fairly suggest a method of reducing radiation resistance or drug resistance in a human cell in vivo, or a method of treating a person with a disease involving resistance to radiation or drug therapy comprising the administration of an antisense that targets HER-2 and inhibits HER-2 expression, nor does the prior art of record teach or fairly suggest an antisense consisting of SEQ ID NO: 3.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Examiner's Comments

The instant disclosure and art teach a relationship between HER-2 overexpression and increases in neoplastic cellular resistance to radiation and drug treatment, wherein down regulation of HER-2 (e.g. inhibition of HER-2 expression) leads to increases in radiation and drug responsiveness of neoplastic cells. HER-2 regulates downstream cell signaling pathways that in turn regulate programmed cell death, and these downstream pathways include multiple signaling cascades that are involved in developing chemoresistance in host cancer cells. These signaling cascades that are downstream of HER-2 and are involved in increasing drug resistance of host cells include, among others, participation of raf-1, Ha-ras, ERK1 and 2, MEKK, MAP2

and 4, and MAPK. Inhibition of HER-2 expression using antisense has been demonstrated in a variety of cancer cells in vitro and in vivo and in appropriate animal models, by both direct and systemic administration of antisense.


Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

3-30-04


RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER